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EXAMINER	
AEDER, SEAN E	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 07/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/510,507	TERRETT, JONATHAN ALEXANDER	
	Examiner	Art Unit	
	Sean E. Aeder, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *1-10 and 12-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

The Election filed 6/8/06 in response to the Office Action of 5/10/06 is acknowledged and has been entered. Applicant elected group IX, drawn to a method for the treatment of carcinoma comprising administering an antibody, and colon cancer with traverse.

The traversal is on the ground(s) that a search and examination of all of the inventions would not impose a serious burden on the examiner. Applicant argues that the groups designated in the Office Action of 5/10/06 fail to define compositions with properties so distinct as to warrant separate examination and search. This is not found persuasive. MPEP 802.01 provides that restriction is proper between inventions which are independent or distinct. It is noted that the instant application is a national stage entry of a PCT, filed under 371 and not 111. As set forth in the Office Action of 5/10/06, the application contains fifteen groups of inventions, which are not so linked to form a single general inventive concept under PCT Rule 13.1. The inventions of the various groups are distinct for the reasons set forth in the Office Action. Each of the groups outlined in the restriction include distinct methods of screening and diagnosing, distinct methods of monitoring, distinct methods of treating, distinct antibodies, and distinct kits. Each of the method inventions is further unrelated as they comprise distinct steps and utilize different products which demonstrates that each method has a different mode of operation. Searching and examining each of these methods would result in a serious burden on the examiner. Further, each of the product inventions are unrelated because each are made by materially different methods, and are used in materially different

methods which have different modes of operation, different functions and different effects. Furthermore, it is noted that the literature search, particularly relevant in this art, is not coextensive and is very important in evaluating the burden of search. Different searches and issues are involved in the examination of each group. For these reasons the restriction requirement is deemed to be proper and is therefore made FINAL.

Claims 1-20 are pending.

Claims 1-10 and 12-20 are withdrawn from further consideration by the examiner under 37 CFR 1.142(b) as being drawn to a non-elected invention.

Claim 11 is currently under consideration.

Claim Objections

Claim 11 is objected to for being dependent upon limitations of unelected claims. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 11 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 11 is rejected as vague and indefinite for being dependent upon claims reciting the term RAIG1 as the sole means of identifying the antibody of claimed method. The use of laboratory designations only to identify a particular molecule renders the claims indefinite because different laboratories may use the same laboratory designations to define completely distinct molecules. Amending the claims to specifically and uniquely identify RAIG1 by SEQ ID Nos can obviate the rejection.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 11 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In the instant case, the claims are inclusive of a genus of antibodies that specifically bind to one or more polypeptides which comprise or consist of the amino acid sequence of SEQ ID NO:1 or a variant or fragment thereof. However, the written description in this case only sets forth antibodies that bind to proteins consisting of the polypeptide sequence set-forth in SEQ ID NO:1. The specification does not disclose every antibody which binds to one or more polypeptides which comprise or consist of variants or fragments of SEQ ID NO:1, as broadly encompassed by the claim.

The specification discloses SEQ ID NO:1 and antibodies that bind to proteins consisting of the polypeptide sequence set-forth in SEQ ID NO:1. Claim 11 does not require that the antibodies possess any particular biological activity, nor any particular conserved structure, or other disclosed distinguishing feature. Further, claim 11 does not require the sequence to which the antibodies specifically bind have any particular conserved structure or other distinguishing feature. Therefore, the written description only reasonably conveys antibodies that bind to proteins consisting of the polypeptide sequence set-forth in SEQ ID NO:1. A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or by describing structural features common to that genus that "constitute a substantial portion of the genus." See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997): "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNA, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus."

The court has since clarified that this standard applies to compounds other than cDNAs. See University of Rochester v. G.D. Searle & Co., Inc., F.3d, 2004 WL 260813, at *9 (Fed.Cir.Feb. 13, 2004). The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features that are common to the genus. That is, the specification provides neither a representative number of antibodies that encompass the genus of antibodies that specifically bind to

one or more RAIG1 polypeptides which comprise or consist of the amino acid sequence of SEQ ID NO:1 or a variant or fragment thereof nor does it provide a description of structural features that are common to said antibodies. Since the disclosure fails to describe common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the disclosure of SEQ ID NO:1 is insufficient to describe the genus. Thus, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of antibodies that specifically bind to one or more RAIG1 polypeptides which comprise or consist of the amino acid sequence of SEQ ID NO:1 or a variant or fragment thereof, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolation. The compound

itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only an antibody wherein said antibody specifically binds to proteins consisting of the polypeptide sequence set-forth in SEQ ID NO:1, but not the full breadth of the claims, meets the written description provision of 35 U.S.C. 112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim 11 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re* Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue."

These factors include, but are not limited to: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention based on the content of the disclosure. See also *Ex parte* Forman, 230 USPQ 546 (BPAI 1986).

The claim recites a method for treatment of colon cancer comprising administering an antibody that specifically binds to one or more polypeptides which comprise or consist of the amino acid sequence of SEQ ID NO:1 or a variant or fragment thereof. It is noted that the specification defines "treatment" as both therapeutic and prophylactic therapy. Thus, the claims are broadly drawn to a method for both therapeutic and prophylactic therapy of colon cancer comprising administering an antibody that specifically binds to one or more polypeptides which comprise or consist of the amino acid sequence of SEQ ID NO:1 or a variant or fragment thereof

The specification discloses that the mRNA encoding SEQ ID NO:1 is overexpressed in colon cancer tissues as compared to normal colon tissue (Figure 4, in particular). The specification also prophetically describes a method for treatment of colon cancer comprising administering an antibody that specifically binds to one or more polypeptides which comprise or consist of the amino acid sequence of SEQ ID NO:1 or a variant or fragment thereof (pages 19-20, in particular). However, the specification lacks working examples demonstrating that any antibody of the claimed method would

treat colon cancer with any predictability of success. As set forth below, this invention is highly unpredictable.

Those of skill in the art recognize the unpredictability of treating tumors with antibodies. For example, Jain (Scientific American July 1994), discloses barriers to the delivery of drugs into solid tumors. These impediments include (1) Non-uniform blood delivery to all areas of the tumor in which some areas of the tumor receive therapeutic agents and other areas of the tumor receive no therapeutic agent at all (page 60 column 3, in particular); (2) Increased viscosity of blood in the tumor itself which also hinders drug delivery to the tumor (see paragraph bridging pages 60 and 61); (3) High liquid pressures in the interstitial matrix can retard the delivery of large therapeutic agents, such as antibodies, into tumors (page 61 column 1 paragraph 1, in particular); (4) Convection is a necessary mechanism by which larger therapeutic molecules such as antibodies reach target cells which are not directly fed by the vasculature. Convection is not observed in large tumors (defined as more than ½ centimeter in diameter, page 62 column 1) and convection is necessary for adequate drug delivery of molecules having a molecular weight of more than 5000 (page 61 column 1through page 63 column 3) and (4) Molecules as large as antibodies (i.e., MW=150,000) would require several months to reach a uniform concentration in a tumor that measures 1 centimeter in radius (page 63 column 2). Further, in the late 80's, Dillman (Annals of Internal Medicine, Volume 111, pages 592-603, 1989) summarized (see abstract) the status of in-vivo use of monoclonal antibodies for treating cancer wherein despite advances in biotechnology, many major hurdles persist including tumor cell heterogeneity, lack of

cytotoxicity, and the development of human anti-mouse antibodies (HAMA). More recently, Weiner (Seminars Oncology, Vol. 26, No. 4, 1999, pages 41-50) provided an overview of monoclonal antibody therapy including some promising activity, however major obstacles to clinical efficacy still exist extending the unpredictability of this treatment. This includes impaired distribution and delivery of antibody to the tumor site, inadequate trafficking of potential cellular effectors to tumor, antigenic heterogeneity, shed or internalized targets, insufficient target specificity, and induction of HAMA (page 43).

Further, treatment of cancer in general is at most unpredictable, as underscored by Gura (Science, 1997, 278:1041-1042.) who discusses the potential shortcoming of potential anti-cancer agents including extrapolating from in-vitro to in-vivo protocols, the problems of drug testing in knockout mice, and problems associated with cologenic assays. Indeed, since formal screening began in 1955, thousands of drugs have shown activity in either cell or animal models, but only 39 that are used exclusively for chemotherapy, as opposed to supportive care, have won approval from the FDA (page 1041 first column, in particular) wherein the fundamental problem in drug discovery for cancer is that the model systems are **not predictive**.

Further, in regards to a method of prophylactic therapy for colon cancer, is well known in the art that the prevention of cancer, in general, is highly unpredictable and Applicant have not demonstrated, with any predictability, that the claimed antibodies would predictably prevent the occurrence of colon cancer. Reasonable guidance with respect to preventing any cancer relies on quantitative analysis from defined

populations; some of which have been successfully pre-screened and are predisposed to particular types of cancer. This type of data might be derived from widespread genetic analysis, cancer clusters, family histories, or randomized controlled trials. For example, Byers, T. (CA Journal, Vol. 49, No. 6, Nov/Dec. 1999) teaches that randomized controlled trials are commonly regarded as the definitive study for proving causality (1st col., p.358), and that in controlled trials the random assignment of subjects to the intervention eliminates the problems of dietary recalls and controls the effects of both known and unknown confounding factors. Further, Byers suggests that chemo-preventative trials be designed "long-term" such that testing occurs over many years (2nd col., p. 359). Further, the essential element towards the validation of any preventive therapeutic is the ability to test the drug on subjects monitored in advance of clinical cancer. This would require monitoring a large population with the claimed agents and *linking* such results with subsequent histological confirmation of the presence or absence of disease.

In view of the teachings above and the lack of guidance, workable examples and or exemplification in the specification, it would require undue experimentation by one of skill in the art to determine with any predictability, that the method would function as claimed.

Summary

No claim is allowed. Claim 11 is rejected under 35 U.S.C. 112, first paragraph, but free of the prior art teaching a method for treatment of colon cancer comprising

administering a therapeutically effective amount of an antibody that specifically binds RAIG1 polypeptide. The closest prior art for claim 11 is Brauner-Osborne et al (Biochimica et Biophysica Acta, 2001, 237-247), which teaches RAIG1 mRNA expression in normal colon tissues; however, this reference does not teach or suggest a method for treatment of colon cancer comprising administering a therapeutically effective amount of an antibody that specifically binds RAIG1 polypeptide.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean E. Aeder, Ph.D. whose telephone number is 571-272-8787. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER